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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/234,208	01/20/1999	JONI KRISTIN DOHERTY	49321-1	6406

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EXAMINER	
UNGAR, SUSAN NMN	
ART UNIT	**PAPER NUMBER**
1642	

MAIL DATE	DELIVERY MODE
05/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/234,208	DOHERTY ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *March 21, 2007, January 26, 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-3,8-10,18-20 and 27-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) ~~27-28~~ is/are allowed. SW

6)☐ Claim(s) *1-3, 8-10, 18-20, 27-30* is/are rejected. SW

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. The Notice of Abandonment mailed May 2, 2007 and the Advisory Action mailed April 17, 2007 are hereby withdrawn. The response filed March 21, 2007 to the Office Action of March 15, 2007 is acknowledged and has been entered. Claims 1-3, 8-10, 18-20, 27-30 are currently pending and currently under consideration. Applicant's remarks and the Declaration filed January 26, 2007 are acknowledged and have been entered and are considered below.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Applicant again requests the transfer of this case to Examiner Anne Holleran for consideration. The request is noted.

4. The following rejections are being maintained:

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3, 8-10, 18-20, 29-30 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed July 26, 2006, Section4, pages 2-9.

Applicant cites case-law, Atlas Powder Co. v E.I. DuPont de Nemours, In re Anderson, In re Marzocci etl al, In re Grimme, Keil and Schmitz, Smith v. Snow, apparently in support of the argument that specific examples of everything within the scope of a broad claim is not required and that every species need not be named in order to enable a claimed invention. The cited case law is noted, however, given

that Applicant has not provided any disclosure of the fact patterns of the cited cases, does not provide a nexus with the fact pattern of the instant invention or point to the reasons why the cited cases are relevant to the instant rejection, the relevance of the case law to the instant rejection can not be evaluated.

Applicant discusses the requirements of 35 USC 112, first paragraph and cites additional case law.

Applicant argues that the specification, in conjunction with that which was known in the art teaches how to make and use the full scope of the claimed invention. In particular, the specification provides general techniques for isolating, expressing and testing polypeptides and any necessary adjustments can be determined empirically using routine testing. The argument has been considered but has not been found persuasive because the requirement under 35 USC 112 first paragraph is not that the specification teach how to test polypeptides, that is to screen for polypeptides having the claimed activity, but rather the requirement under 35 USC 112 first paragraph is that the specification teach how to make the claimed invention. In particular, screening assays do not enable the claimed invention because the court found in (*Rochester v. Searle*, 358 F.3d 916, Fed Cir., 2004) that screening assays are not sufficient to enable an invention because they are merely a wish or plan for obtaining the claimed chemical invention.

Applicant argues that the claims are clearly within the scope of what is taught in the specification, that is a genus of polypeptides of p68HER-2 that includes the claimed polypeptides and points out that the specification teaches that both p68HER-2 and a fragment thereof of 79 amino acids binds to the ECD of HER-2 and provides detailed assays for assessing their binding affinity and that these assays are recognized by one of skill in the art and by following the teachings

of the specification, one of skill in the art can readily make the claimed polypeptides and measure their binding affinity. The argument has been considered but has not been found persuasive because although the claims are clearly within the scope of what is taught in the specification, the scope of those claims is not enabled for the reasons of record and further, as set forth above, the requirement under 35 USC 112 first paragraph is not that the specification teach how to test polypeptides, that is to screen for polypeptides having the claimed activity, but rather the requirement under 35 USC 112 first paragraph is that the specification teach how to make the claimed invention. In particular, screening assays do not enable the claimed invention because the court found in (*Rochester v. Searle*, 358 F.3d 916, Fed Cir., 2004) that screening assays are not sufficient to enable an invention because they are merely a wish or plan for obtaining the claimed chemical invention.

Applicant argues that the level of skill in this art is recognized as high and numerous articles and patents made of record address a highly skilled audience and further evidence the high level of skill in this art. The argument has been considered but has not been found persuasive because although the specification teaches how to screen for the instant invention, the specification does not meet the requirements of 35 USC 112, first paragraph for the reasons set forth previously and above.

Applicant argues that at the time of filing there was a broad body of knowledge drawn to HER-2 and other tyrosine kinases and that truncated variants of ECD of a variety of HER family RTKs was known and analyzed for function which demonstrates that identification, production and/or analysis of truncated RTK precuts, including truncated HER-2 polypeptides and analysis of these

peptides was well known in the art. The argument has been considered but has not been found persuasive because although the art teaches how to screen for activity, the instant application does not meet the requirements of 35 USC 112, first paragraph for the reasons set forth previously and above.

Applicant reiterates arguments drawn to the genus of p68HER-2 polypeptides and fragments that bind with high affinity to the ECD of HER-2. The argument was considered above and not found to be persuasive for the reasons set forth above.

Applicant reiterates the teachings of the working examples, that is the specification exemplifies how to clone, purify and test the binding affinity of the 79 amino acid fragment of p68HER-2 and further exemplifies the binding of p68HER2 to HER-2 and exemplifies that the binding affinity of p68HER-2 resides in the novel praline rich ECDIIIa region, apparently suggesting that the working examples enable the broadly claimed invention. It is noted however, that the working examples are not drawn to the broadly claimed invention, and for the reasons of record drawn to the unpredictability of protein chemistry, the scope of the claimed invention is not enabled.

Applicant argues that given the extensive teaching in the specification, given what was known in the art at the time the instant application was filed, it is not unpredictable that the claimed variants can be generated and tested for their ability to bind HER-2. The argument has been considered but has not been found persuasive for the reasons previously set forth drawn to the unpredictability of protein chemistry and further, as set forth above, the requirement under 35 USC 112 first paragraph is not that the specification teach how to test polypeptides, that is to screen for polypeptides having the claimed activity, but rather the requirement

under 35 USC 112 first paragraph is that the specification teach how to make the claimed invention. In particular, screening assays do not enable the claimed invention because the court found in (*Rochester v. Searle*, 358 F.3d 916, Fed Cir., 2004) that screening assays are not sufficient to enable an invention because they are merely a wish or plan for obtaining the claimed chemical invention.

Applicant argues that Examiner's rejections drawn to the unpredictability of protein chemistry the lack of teaching of critical amino acids and the effects of truncations and additions on SEQ ID NO:1 or SEQ ID NO:2 are not relevant to the instant issue under consideration because the claims are drawn to variants that bind HER-2 with very high affinity and this functional limitation naturally excludes polypeptides that would not bind to HER-2. The argument has been considered but has not been found persuasive because the rejections are very much relevant to the issue raised because the specification for the reasons set forth previously and above does not teach how to make the claimed variants that will bind to HER-2 with very high affinity and function as claimed.

Applicant reiterates arguments drawn to the teaching of the entire sequence of the polypeptide and assays for screening. Applicant argues that one could systematically remove residues and if necessary test for activity. The argument has been considered but has not been found persuasive because the claims as currently constituted are not limited to truncations of p68HER-2 and further remain rejected for the reasons set forth previously and above.

Applicant argues that not only SEQ ID NO:2 (which comprises SEQ ID NO:1) but also HIS tagged SEQ ID NO:1 bind to HER-2 and thus it is not unpredictable that other polypeptide fragments also bind and that screening assays could test the ability of polypeptides to bind. The argument has been considered

but has not been found persuasive because as set forth above, the requirement under 35 USC 112 first paragraph is that the specification teach how to make the claimed invention. In particular, screening assays do not enable the claimed invention because the court found in (*Rochester v. Searle*, 358 F.3d 916, Fed Cir., 2004) that screening assays are not sufficient to enable an invention because they are merely a wish or plan for obtaining the claimed chemical invention.

Applicant argues that the claims refer to contiguous residues which should address much of the Examiner's concern. The argument has been considered but has not been found persuasive because, the issue raised is not drawn to contiguous residues, but rather is drawn to the unpredictability of protein chemistry.

Applicant argues that SEQ ID NO:1 and SEQ ID NO:2 bind with very high affinity to HER-2 and that given that the 79 amino acid subregion binds, this would not suggest to one skilled in the art that the entire 79 amino acids are essential for high affinity binding but rather only that the minimal region sufficient for binding is contained therein and therefore Applicants have justifiably claimed a somewhat smaller contiguous region, limited by the functional proviso that the region must still demonstrate high-affinity binding (at least 10^8M^{-1}).

The argument has been considered but has not been found persuasive because, as previously set forth, the specification as originally filed fails to teach the amino acids critical to the claimed invention and given the unpredictability of the protein chemistry arts, the claimed invention does not meet the scope requirements of 35 USC 112, first paragraph for the reasons of record. Further, it is noted that a review of the specification does not reveal any disclosure of, suggestion for, guidance on a "minimal region sufficient for binding".

Applicant argues that in further confirmation of the reasonable basis for

claiming regions of at least 50 contiguous amino acids, several of applicants' copending applications disclose specific active polymorphic variants of HERSTATIN that correspond to non-conservative amino acid substitutions. Significantly, 6 of these non-conservative variable positions occur within the first 21 amino acid positions. This finding confirms the instant teachings and disclosure that the minimal binding region is contained in a subregion of ECDIIIA (e.g. 50 to 79 residues). The argument has been considered but has not been found persuasive because there is no teaching in the specification as originally filed drawn to "the minimal binding region" and no teaching of the amino acids critical to the claimed invention or teaching of variants with non-conservative amino acid substitutions within the first 21 amino acid positions that function as claimed.

Applicant argues that the instant specification teaches heterologous fusion proteins with the ECDIIIa region. In particular, the specification teaches that SEQ ID NO:1 produced and used in Example 9 was a fusion protein of SEQ ID NO:1 which comprised a heterologous amino terminal region of about 50 amino acids, therefore, Applicants have not only disclosed a smaller contiguous binding region but have demonstrated its function in the context of a much larger polypeptide, namely SEQ ID NO:2 and more significantly a sizable diverse fusion protein. The argument has been considered but has not been found persuasive, because although Applicant has demonstrated the binding of a single HIS tagged SEQ ID NO:1, this does not enable the scope of the broadly claimed invention and this binding is not persuasive for the reasons previously set forth and because of the unpredictability of the protein chemistry arts.

Applicant argues that the Clinton Affidavit addresses Examiner's concern in the absence of knowing the residues of SEQ ID NO:1 that are critical to binding,

wherein truncation would be expected to alter the conformation of the claimed polypeptides. Applicant argues that Applicants did know, based on a hydrophobicity analysis done in 1998, what residues would be expected to be important for folding and binding activity and that this knowledge provided the conceptual support for and was memorialized in the claimed recitation of 50 to 79 contiguous amino acid residues of SEQ ID NO:1. Applicant further argues this information was regarded as critical to binding activity as well as for protein folding and binding activity of SEQ ID NO:1 subdomains that comprised the hydrophobic subdomain. Therefore the basis of explicitly claiming subfragments of 50 to 79 contiguous amino acids followed from the central position of the hydrophobic residues amino acids 32-48 within the 79 amino acid SEQ ID NO:1 and the fact that such hydrophobic regions were widely recognized in the art to be generally critical for protein folding and protein-protein interactions. This aspect of the conception was that the smallest contiguous fragment that yet included the hydrophobic domain would reasonably be able to fold properly and bind. It was appreciated by Applicants at the time that any contiguous stretch of 50 contiguous amino acids, regardless of where such stretch is located within SEQ ID NO:1 will include the central hydrophobic domain.

The argument has been considered but has not been found persuasive because although Applicant might have had information obtained in 1998, that information was not shared with those of ordinary skill in the specification as originally filed. Further, as previously set forth, contrary to Applicant's argument, those of ordinary skill in the art recognize that even a single minor amino acid change in a binding protein can dramatically alter binding activity and affinity.

It is noted that a review of the Clinton Affidavit reveals that Dr. Clinton does

indeed state that the instant claims were reasonably encompassed within the original conception of the presently claimed subject matter and that Dr. Clinton discloses information drawn to hydrophobicity analysis not presented in the specification as originally filed.

Applicant further argues that a deficiency in meeting one of the Wand's factors does not preclude a finding of enablement and that predictability is only one factor. The claimed subject matters require that the polypeptides bind to the ECD of HER-2 with a specified binding affinity and that the skill of those in the art could predictably generate polypeptides as claimed.

The argument has been considered but has not been found persuasive because in the absence of teachings drawn to the critical amino acids required for making the claimed invention, one would not be able to predictably make the claimed invention, that is, to predictably distinguish between those polypeptides that will function as claimed and those that will not.

Applicant further argues that reliance on *Rochester v. Searle* is misplaced because Rochester addresses written description and not enablement which is distinct. In addition, the facts pertinent to the findings in *Rochester v. Searle* are distinct from the instant claims. The claims at issue in Rochester were directed to screening assays for use in determining whether a particular drug inhibited the activity of COX-2 without inhibiting COX-1. The '850 patent did not disclose any compound that would function as claimed nor provide any suggestion as to how such a compound could be made or otherwise obtained other than by trial and error research and thus the court concluded that the patent lacked adequate written description.

The argument has been considered but has not been found persuasive

because although the written description and enablement rejections have been found to be distinct wherein it can be found that written description is found while enablement is not or that enablement is found, even though the invention is not described, and the analysis of these two provisions is different, considerable overlap has been found in decisions involving written description and enablement. Further, although the findings in Rochester are drawn to written description and not to enablement, it is clear that written description is in fact critical to the enablement of these claims. Further, although the fact patterns of the two cases are not identical, and although Applicant presents information drawn to two closely related structures that would be expected to function as claimed, in point of fact and as repeatedly stressed by Applicant (see above) the making of the claimed variants is completely dependent upon screening assays which will identify the uncharacterized structures that will function as claimed. Thus, although not identical in fact pattern, the essential features of the two cases are indeed the same, (1) both cases are drawn to drugs effective for treatment, (2) both cases are drawn to specific structures that have not been identified, (3) both bases require that screening assays be used to identify the structures that would be expected to function as claimed.

Applicant goes on to discuss the Rochester case in detail stating that "because the Federal Circuit affirmed the district court's decision on the written description ground, it 'considere[ed] the enablement issue to be moot". Thus it appears that the court agrees with Examiner's analysis that given that the written description was inadequate, in the absence of complying with the written description requirement, enablement issues are moot, that is the claims are clearly not enabled.

Applicant argues that in contrast to Rochester, the instant claims are drawn to polypeptides which are disclosed in the specification and Applicant reiterates the arguments drawn to the genus represented by SEQ ID NO:1 or SEQID NO:2. Applicant further argues that testing polypeptides for activity is routine and readily achieved, and again points to the hydrophobicity information known to Dr. Gail Clinton in 1998 but not revealed in the specification as originally filed. Applicant concludes the argument by stating that the findings in Rochester v. Searle are not on point and inapt with respect to the instantly claimed subject matter. The argument has been considered but has not been found persuasive because the particular polypeptides broadly claimed are not in fact disclosed in the specification. Further, as drawn to the genus argument, for the reasons set forth above, this argument is not convincing. As drawn to the screening arguments, it is clear that screening, identical to the Rochester case, is critical to the claimed invention and the arguments for the reasons set forth above, are not persuasive. Finally, the hydrophobicity information, known to Dr. Clinton in 1998, was not revealed to those of ordinary skill in the art at the time the application was submitted and not mentioned in the specification as originally filed.

Applicant's statement on public policy considerations is noted.

The arguments have been carefully considered but have not been found persuasive and the rejection is maintained.

7. Claims 18-20, 29-30 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed July 26, 2006, Section 5, pages 10-11.

Applicant argues that for the reasons set forth above, it would not require undue experimentation for a person of skill in the art to make and use the claimed

pharmaceutical compositions. Applicant points specifically to anti-tumor cell activity by p68HER-2 in an assay of assessing anchorage independent growth of cells in soft agar on p. 13, lines 5-23 and that given the high degree of knowledge that was available at the time of the filing of the instant application in combination with the teachings of the specification, the broadly claimed invention is enabled. The argument has been considered but has not been found persuasive because the issue raised is not drawn to SEQ ID NO:2/p68HER-2 which was used in the assay disclosed on p. 13, lines 5-23, but rather is drawn to the claims that include polypeptides comprising fragments of SEQ ID NO:2, comprising SEQ ID NO:1 and fragments of SEQ ID NO:1. For the reasons previously set forth the specification as originally filed is not enabling for a pharmaceutical composition comprising species other than p68HER-2/SEQ ID NO:2.

Applicant argues that the Examiner has provided no evidence that the polypeptides cannot be formulated as a pharmaceutical composition and so used. Applicant further argues that the claims recite that the polypeptides have a recited binding affinity which the exemplified polypeptides possess. The argument has been considered but has not been found persuasive because although it is clear that the polypeptides can be formulated as pharmaceutical compositions, the art recognizes the unpredictability of the cancer treatment arts contemplated in the specification and in the absence of objective evidence, for the reasons previously set forth, no one of ordinary skill in the art would believe it more likely than not that the broadly claimed invention would function as claimed.

The arguments have been considered but have not been found persuasive and the rejection is maintained.

8. Claims 8-10, 18, 29-30 remain rejected under 35 USC 112, first paragraph

for the reasons previously set forth in the paper mailed July 26, 2006, Section 6, page 11.

Applicant argues that the original specification describes a genus of compounds that comprises SEQ ID NO:1 or 50-79 contiguous amino acid-containing fragments thereof and that bind at nanomolar concentrations meaning that they would have a binding affinity of at least 10^8 as recited. Applicant further argues that both SEQ ID NO:1 and SEQ ID NO:2 are encompassed by the genus of compounds and that the specification states at page 8 that the unique ECDIIIa peptide binds with high affinity (nM concentrations to HER-2) providing support for the nM affinity of SEQ ID NO:1. Further, Applicant argues that the legend to Figure 7 describes the use of nanomolar concentrations of SEQ ID NO:2 for binding to SKOV-3 cells and that this provides support for nM affinity of SEQ ID NO;2. The argument has been considered but has not been found persuasive because although the specification teaches that nanomolar concentrations of SEQ ID NO:2 for binding to SKOV-3 cells were used, this does not in fact provide information drawn to the actual affinity binding constant of the polypeptide for HER-2. Further, although the specification teaches nM concentrations for high affinity binding of SEQ ID NO:1 to HER-2, the issue raised is not drawn to the affinity of SEQ ID NO:1. Although Applicant argues that the polypeptides comprising fragments are encompassed by the genus of compounds represented by SEQ ID NO:1 and SEQ ID NO:2, this does not perfect the teaching of the specification which does not support Applicant's contention drawn to the affinity of SEQ ID NO:2 or fragments thereof other than SEQ ID NO:1.

The argument has been considered but has not been found persuasive and the rejection is maintained.

9. Claims 8-10, 18 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed July 26, 2006, Section 7, page 12.

Applicant argues that there is explicit literal support for the limitation of at least one glycosylation site in the specification at page 5, line 23 and at page 16, line 5 wherein the specification describes "a consensus asparagine linked glycosylation site". The argument has been considered but has not been found persuasive because contrary to Applicant's argument, the specification does not provide explicit support for the limitation at either cite. In particular, a review of page 5, line 20 of the specification reveals support for "The novel 79 amino acid sequence.....has **a** (emphasis added) consensus asparagine linked glycosylation site, which is underlined" and a review of page 16, line 5 did not reveal any mention of a consensus sequence or a glycosylation site. It is noted that claim 8 is drawn to "SEQ ID NO:2 or a fragment of SEQ ID NO:2 from about 80 to 419 contiguous residues in length wherein the C terminal 79 contiguous amino acids are present, wherein **at least one** (emphasis added) N-linked glycosylation site is present". The cited support is drawn only to the novel 79 amino acid sequence and not to either SEQ ID NO;2 or a fragment of SEQ ID NO:2 from about 80 to 419 contiguous residues in length and in particular is not drawn to "at least one" N-linked glycosylation site.

Applicant further argues that the specification teaches that there is disclosure in the specification for "at least three N-linked glycosylation sites" as well as the ECD portion of HERSTATIN containing five N-glycosylation sites and that the novel 79 aa portion contains one consensus N-linked glycosylation site. Thus a polypeptide of 80-419 amino acids that contains the 79 amino acid portion has "at least one' N-linked glycosylation site present and depending on the length of the

polypeptide, other N-linked glycosylation sites can also be present. The argument has been considered but although it would appear that the claimed polypeptide would have at least one glycosylation site, this limitation was not contemplated in the specification as originally filed and the claimed limitation broadens the scope of the invention as originally filed because the specification never contemplated any polypeptide or fragment of SEQ ID NO:2 from about 80 to 419 contiguous residues in length that had only a single glycosylation site, as encompassed by the claims. Again other than specifically the 79 amino acid portion that has one N-glycosylation site no range of amino acids is disclosed to have a single N-linked gycosylation site and clearly no range of amino acids is disclosed to have "at least one" glycosylation site.

Further it is noted that a review of the specification reveals that the "at least three N-linked glycosylation sites" are found specifically at page three of the specification, lines 14-21 wherein the three sites are drawn to a polypeptide having from 80 to 419 amino acids taken from the sequence of SEQ ID NO:2, wherein the C terminal 79 amino acids are present. Here again, there is no recitation or contemplation of the sequence having "at least one" one N-linked glycosylation site.

The argument has been considered but has not been persuasive and the rejection is maintained.

10. Claims 18 and 30 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed July 26, 2006, Section 8, pages 12-13.

Applicant argues that there is explicit literal support for this limitation on page 9, line 21 through page 10, line 9. The argument has been considered but has

not been found persuasive because contrary to Applicant's argument, the specification does not provide explicit support for the limitation at this cite. Nowhere in the suggested support is there found a recitation of the proviso "combinations thereof, with the proviso that where the composition comprises the monoclonal antibody it also comprises at least one of the agents of (a) and (b)". The specification as originally filed supports only "combinations thereof, with the proviso that the agent cannot be the monoclonal antibody alone". There is a clear difference in scope between the teaching of the specification and the claims as currently constituted. Although Applicant argues that the claim cannot be interpreted as allowing the antibody to be in combination with any second agent, this is because combination thereof must be combinations thereof, that is of (a) (b) and (c) and not combination of (c) with any second agent that is not (a) or (b). The argument has been considered but has not been persuasive because the recitation of the phrase "at least" opens the scope of the claimed invention so that the claimed invention is not limited, as originally taught in the specification to "combinations thereof, with the proviso that the agent cannot be the monoclonal antibody alone" but now as claimed, the composition comprises the monoclonal antibody and at least one of the agents of (a) and (b) without limiting the additional agents to only (a) and (b).

The argument has been considered but has not been found persuasive and the rejection is maintained.

11. Claim 9 remains rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed July 26, 2006, Section 9, page 12.

Because applicant did not distinctly and specifically point out the supposed errors in the rejection, the rejection is maintained.

12. All other objections and rejections set forth in the previous office action are hereby withdrawn. Claims 27 + 28 Appear to be free of the art and Allowable. Su

13. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley, can be reached at 571-272-0898. The fax phone number for this Art Unit is (571) 273-8300.

Susan Ungar
Primary Patent Examiner
May 23, 2007